

**AMENDMENTS TO THE CLAIMS:**

This listing of claims will replace all prior versions, and listings, of claims in the application:

**LISTING OF CLAIMS:**

Claim 1 (Currently Amended) A mucoadhesive polymer comprising not more than 10 different monomers and at least one non-terminal thiol group, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers.

Claims 2-27 (Canceled).

Claim 28 (Previously Presented) A polymer as set forth in claim 1, said polymer comprising at least 0.05  $\mu$ mol of covalently bound thiol groups per gram of polymer.

Claim 29 (Previously Presented) A polymer as set forth in claim 1, said polymer comprising at least 0.1  $\mu$ mol of covalently bound thiol groups per gram of polymer.

Claim 30 (Canceled).

Claim 31 (Currently Amended) A polymer as set forth in claim 1, wherein said ~~thiol groups are cysteine groups~~ polymer comprises at least one cysteine group.

Claim 32 (Currently Amended) A polymer as set forth in claim 31, wherein said ~~cysteine groups are~~ at least one cysteine group is bound to said polymer via an amide bond.

Claim 33 (Previously Presented) A polymer as set forth in claim 1, wherein said polymer includes at least one monomer having free thiol groups within said polymer.

Claim 34 (Canceled).

Claim 35 (Previously Presented) A polymer as set forth in claim 1, said polymer exhibiting a total work of adhesion (TWA) of more than 150  $\mu$ J to intestinal mucosa at a pH of 7.

Claim 36 (Previously Presented) A polymer as set forth in claim 1, said polymer exhibiting a total work of adhesion (TWA) increased by at least 30% relative to a mucoadhesive polymer not containing at least one non-terminal thiol group,

measured at a pH optimum of the total work of adhesion (TWA) of the thiolated polymer.

Claim 37 (Previously Presented) A polymer as set forth in claim 1, said polymer exhibiting a total work of adhesion (TWA) increased by at least 50% relative to a mucoadhesive polymer not containing at least one non-terminal thiol group, measured at a pH optimum of the total work of adhesion (TWA) of the thiolated polymer.

Claim 38 (Previously Presented) A polymer as set forth in claim 1, said polymer exhibiting a total work of adhesion (TWA) increased by at least 100% relative to a mucoadhesive polymer not containing at least one non-terminal thiol group, measured at a pH optimum of the total work of adhesion (TWA) of the thiolated polymer.

Claim 39 (Withdrawn) A pharmaceutical composition comprising a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group, and at least one active substance capable of being taken up via mucosae, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer

of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers.

Claim 40 (Withdrawn) A pharmaceutical composition as set forth in claim 39, wherein said active substance is non-covalently bound to said polymer.

Claim 41 (Withdrawn) A pharmaceutical composition as set forth in claim 39, said pharmaceutical composition being provided in a form selected from the group consisting of a tablet, a suppository, a pellet, eyedrops, nosedrops, eardrops, an eye-gel, a nose-gel, an ear-gel, an application for inhalation, microparticles and nanoparticles.

Claim 42 (Withdrawn) A pharmaceutical composition as set forth in claim 39, wherein said active substance is a substance whose activity is enhanced by thiol groups.

Claim 43 (Withdrawn) A pharmaceutical composition as set forth in claim 42, wherein said active substance enhanced by thiol groups is a thiol-dependent enzyme.

Claim 44 (Withdrawn) A pharmaceutical composition as set forth in claim 43, wherein said thiol-dependent enzyme is selected from the group consisting of papain and subtilisin.

Claim 45 (Withdrawn) A pharmaceutical composition as set forth in claim 39, wherein said composition is in a form suitable for peroral administration.

Claim 46 (Withdrawn) A pharmaceutical composition as set forth in claim 39, wherein said active substance is in a form suitable for delayed release.

Claim 47 (Withdrawn) A pharmaceutical composition as set forth in claim 46, wherein said active substance is present within a polymer tablet and said active substance is capable of penetrating through the polymer coat upon administration to a patient.

Claim 48 (Withdrawn) A method of enhancing permeation of active substances through mucosa in an individual, said method comprising administering to said individual a pharmaceutical composition comprising a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group in an amount effective for enhancing permeation of active substances, and at least one active substance capable of being taken up via a mucosa in a therapeutically effective amount, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers.

Claim 49 (Withdrawn) A method as set forth in claim 48, wherein said pharmaceutical composition comprises an active (poly)peptide substance.

Claim 50 (Withdrawn) A method of enhancing permeation of active substances through mucosa in an individual, said method comprising administering to said individual a pharmaceutical composition comprising a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group in an amount effective for enhancing permeation of active substances, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers ~~wherein said mucoadhesive polymer is selected from the group consisting of a thiolated copolymer of acrylic acid and divinyl glycol, thiolated chitosan, thiolated sodium carboxymethylcellulose, thiolated sodium alginate, thiolated sodium hydroxypropylcellulose, thiolated hyaluronic acid, thiolated pectin and derivatives of these thiolated polymers, and~~  
at least one active substance capable of being taken up via a mucosa in a therapeutically effective amount.

Claim 51 (Withdrawn) A method according to claim 50, wherein said thiol ~~groups are cysteine groups~~ polymer comprises at least one cysteine group.

Claim 52 (Withdrawn) A method as set forth in claim 50, wherein said mucosa is an intestinal mucosa.

Claim 53 (Withdrawn) A method of administering an active ingredient to an individual in need thereof wherein the active ingredient is taken up via mucosae, said method comprising administering to said individual a pharmaceutical composition comprising a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers, in an amount effective to introduce an active substance to said mucosae, and  
at least one active substance to be taken up via mucosae in a therapeutically effective amount, wherein said active ingredient is capable of adhering to a mucosa selected from the group consisting of intradermal, intraocular and intraarticular mucosa.

Claim 54 (Withdrawn) A method of inhibiting enzymes in an individual, said method comprising administering to said individual a pharmaceutical composition which comprises a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers, and

at least one active substance capable of inhibiting enzymes in an amount effective for inhibiting said enzymes.

Claim 55 (Withdrawn) A method of inhibiting zinc ion-dependent enzymes in an individual, said method comprising administering to said individual a pharmaceutical composition which comprises a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers,



and at least one active substance capable of inhibiting zinc ion-dependent enzymes in an amount effective for inhibiting said enzymes.

Claim 56 (Withdrawn) A method of preparing a mucoadhesive polymer, said method comprising

providing base polymers assembled of not more than 10 different monomers, wherein at least one of the non-terminal monomers includes a terminal, functional group I, said functional group I being free within said polymer,

providing thiol-containing compounds, said thiol-containing compounds including at least one further functional group II, wherein said functional groups I and II are together capable of forming a covalent bond, and

reacting said base polymers with said thiol-containing groups, said functional group I thereby forming a covalent bond with said functional group II,

said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers.

Claim 57 (Withdrawn) A method as set forth in claim 56, further comprising adding coupling reagents when reacting said base polymers with said thiol-containing compounds.

Claim 58 (Withdrawn) A method as set forth in claim 57, wherein said functional group I is a carboxyl group and said functional group II is an amino group.

Claim 59 (Withdrawn) A method as set forth in claim 58, wherein said amino group is a primary amino group.

Claim 60 (Withdrawn) A method as set forth in claim 57, wherein said coupling reagents are carbodiimides, and amide bonds are formed.

Claim 61 (Withdrawn) A method as set forth in claim 56, wherein said thiol-containing compound is a mercapto-compound comprising a primary amino group.

Claim 62 (Withdrawn) A method as set forth in claim 61, wherein said thiol-containing compound is selected from the group consisting of cysteine and a cysteine derivative.

Claim 63 (Withdrawn) A method as set forth in claim 56, wherein said reacting of said base polymers with said thiol-containing groups is performed at a pH of between 4 and 8.

Claim 64 (Withdrawn) A method as set forth in claim 56, wherein said reacting of said base polymers with said thiol-containing groups is performed at a pH of between 5.5 and 6.5.

Claim 65 (Withdrawn) A method as set forth in claim 56, further comprising adjusting said prepared polymer to a pH of between 5 and 9.

Claim 66 (Withdrawn) A method as set forth in claim 56, further comprising adjusting said prepared polymer to a pH of between 6.5 and 8.5.

Claim 67 (Withdrawn) A method of preparing a pharmaceutical composition comprising a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group, said method comprising combining a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group with at least one active substance capable of being taken up via mucosae, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers.

Claim 68 (Withdrawn) A method as set forth in claim 67, wherein said polymer is not covalently bound during said combining of said mucoadhesive polymer with said active substance.

Claim 69 (Withdrawn) A method as set forth in claim 67, wherein said mucoadhesive polymer and said active substance are combined by co-lyophilizing said polymer and said active substance.

Claim 70 (Withdrawn) A method of improving mucoadhesion of a polymer, said method comprising  
introducing laterally arranged thiol groups into a polymer, and  
applying said polymer with said thiol groups introduced thereinto to a mucus layer so as to form disulfide bonds between said polymer and said mucus layer.

Claim 71 (Withdrawn) A method as set forth in claim 53, wherein said pharmaceutical composition further comprises at least one active substance to be taken up via said mucosa.

Claim 72 (Withdrawn) A polymer as set forth in claim 30, wherein said derivatives are selected from the group consisting of derivatives obtained by auto-cross-linking, introduction of functional groups, attachment of complexing agents and coupling of enzyme inhibitors.

Claim 73 (Withdrawn) A polymer as set forth in claim 72, wherein said complexing agent is selected from the group consisting of EDTA.

Claim 74 (Canceled).

Claim 75 (Withdrawn) A polymer as set forth in claim 74, wherein said derivatives are selected from the group consisting of derivatives obtained by auto-cross-linking, introduction of functional groups, attachment of complexing agents and coupling of enzyme inhibitors.

Claim 76 (Withdrawn) A polymer as set forth in claim 75, wherein said complexing agent is selected from the group consisting of EDTA.

Claim 77 (Withdrawn) A polymer as set forth in claim 74, wherein said ~~thiol groups are cysteine groups~~ polymer comprises at least one cysteine group.

Claim 78 (Withdrawn) A polymer as set forth in claim 77, wherein said ~~cysteine groups are~~ at least one cysteine group is bound to said polymer via an amide bond.

Claim 79 (Withdrawn) A polymer as set forth in claim 74, wherein said polymer includes at least one monomer having free thiol groups within said polymer.

Claim 80 (Withdrawn) A polymer as set forth in claim 74, said polymer exhibiting a total work of adhesion (TWA) increased by at least 50% relative to a mucoadhesive polymer not containing at least one non-terminal thiol group, measured at a pH optimum of the total work of adhesion (TWA) of the thiolated polymer.

Claim 81 (Withdrawn) A polymer as set forth in claim 74, said polymer comprising at least 0.1  $\mu\text{mol}$  of covalently bound thiol groups per gram of polymer.

Claim 82 (Withdrawn) A pharmaceutical composition comprising a mucoadhesive polymer having not more than 10 different monomers and at least one non-terminal thiol group, said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu\text{J}$  to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers ~~wherein said polymer is selected from the group consisting of a thiolated copolymer of acrylic acid and divinyl glycol, thiolated chitosan, thiolated sodium carboxymethylcellulose, thiolated sodium alginate, thiolated sodium hydroxypropylcellulose, thiolated hyaluronic acid, thiolated pectin and derivatives of said thiolated polymers, and~~ at least one active substance capable of being taken up via mucosae.

Claim 83 (Withdrawn) A pharmaceutical composition as set forth in claim 82, wherein said active substance is non-covalently bound to said polymer.

Claim 84 (Withdrawn) A pharmaceutical composition as set forth in claim 82, wherein said active substance is a substance whose activity is enhanced by thiol groups.

Claim 85 (Withdrawn) A pharmaceutical composition as set forth in claim 84, wherein said active substance enhanced by thiol groups is a thiol-dependent enzyme.

Claim 86 (Withdrawn) A pharmaceutical composition as set forth in claim 85, wherein said thiol-dependent enzyme is selected from the group consisting of papain and subtilisin.

Claim 87 (Withdrawn) A method of enhancing permeation of active substances through mucosa in an individual, said method comprising administering to said individual a pharmaceutical composition according to claim 82.

Claim 88 (Withdrawn) A method as set forth in claim 87, wherein said pharmaceutical composition comprises an active (poly)peptide substance.

Claim 89 (Withdrawn) A method of administering an active ingredient to an individual in need of an active ingredient which will adhere to a mucosa layer, said method comprising administering to said individual a pharmaceutical composition according to claim 82, wherein said pharmaceutical composition adheres to a mucosa layer selected from the group consisting of intradermal, intraocular and intraarticular mucosa.

Claim 90 (Withdrawn) A method of inhibiting enzymes in an individual, said method comprising administering to said individual a pharmaceutical composition according to claim 82, wherein said active substance is capable of inhibiting enzymes, in an amount effective to inhibit said enzymes.

Claim 91 (Withdrawn) A method of inhibiting zinc ion-dependent enzymes in an individual, said method comprising administering to said individual a pharmaceutical composition according to claim 82, wherein said active substance is capable of inhibiting zinc ion-dependent enzymes, in an amount effective to inhibit said enzymes

Claim 92 (Withdrawn) A method of preparing a mucoadhesive polymer, said method comprising

providing base polymers assembled of not more than 10 different monomers, wherein at least one of the non-terminal monomers includes a terminal, functional group I, said functional group I being free within said polymer and wherein said functional group I is a carboxyl group,

providing thiol-containing compounds, said thiol-containing compounds including at least one further functional group II, wherein said functional group II is an amino group,

reacting said base polymers with said thiol-containing groups, said functional groups I thereby forming a covalent bond with said functional groups II, and obtaining a mucoadhesive polymer,



said polymer exhibiting a total work of adhesion (TWA) of more than 120  $\mu$ J to intestinal mucosa at a pH of 7, and said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of hyaluronic acid, a thiolated polymer of pectin, and derivatives of said thiolated polymers.

Claim 93 (Withdrawn) A method as set forth in claim 92, further comprising adding at least one coupling reagent when reacting said base polymers with said thiol-containing compounds.

Claim 94 (Withdrawn) A method as set forth in claim 92, wherein said amino group is a primary amino group.

Claim 95 (Withdrawn) A method as set forth in claim 93, wherein said coupling reagents are carbodiimides, and amide bonds are formed.

Claim 96 (Withdrawn) A method as set forth in claim 92, wherein said thiol-containing compound is selected from the group consisting of cysteine and a cysteine derivative.

Claim 97 (Withdrawn) A method as set forth in claim 92, wherein said base polymers are reacted with said thiol-containing groups at a pH of between 5.5 and 6.5.

Claim 98 (Withdrawn) A method of improving mucoadhesion of polymers, said method comprising

introducing laterally arranged thiol groups into a polymer having no more than 10 different monomers, and

applying said polymers with said thiol groups introduced therein to a mucus layer so as to form disulfide bonds between said polymer and said mucus layer.

Claim 99 (Withdrawn) A method as set forth in claim 98, wherein said thiolated polymer is selected from the group consisting of a thiolated copolymer of acrylic acid and divinyl glycol, thiolated chitosan, thiolated sodium carboxymethylcellulose, thiolated sodium alginate, thiolated sodium hydroxypropylcellulose, thiolated hyaluronic acid, thiolated pectin and derivatives of said thiolated polymers.

Claim 100 (Withdrawn) In a mucoadhesive polymer comprising not more than 10 different monomers, the improvement comprising said polymer having at least one non-terminal thiol group.

Claim 101 (Withdrawn) The mucoadhesive polymer according to claim 100, wherein said polymer is selected from the group consisting of a thiolated copolymer

of acrylic acid and divinyl glycol, thiolated chitosan, thiolated sodium carboxymethylcellulose, thiolated sodium alginate, thiolated sodium hydroxypropylcellulose, thiolated hyaluronic acid, thiolated pectin and derivatives of said thiolated polymers.

Claim 102 (Withdrawn) A polymer as set forth in claim 101, wherein said derivatives are selected from the group consisting of derivatives obtained by auto-cross-linking, introduction of functional groups, attachment of complexing agents and coupling of enzyme inhibitors.

Claim 103 (Withdrawn) A polymer as set forth in claim 102, wherein said complexing agent is selected from the group consisting of EDTA.

Claim 104 (Withdrawn) A polymer as set forth in claim 100, wherein said ~~thiol groups are cysteine groups~~ polymer comprises at least one cysteine group.

Claim 105 (Withdrawn) A polymer as set forth in claim 104, wherein said ~~cysteine groups are~~ at least one cysteine group is bound to said polymer via an amide bond.

Claim 106 (Withdrawn) A polymer as set forth in claim 100, wherein said polymer includes at least one monomer having free thiol groups within said polymer.

Claim 107 (Withdrawn) A polymer as set forth in claim 100, said polymer exhibiting a total work of adhesion (TWA) increased by at least 50% relative to a mucoadhesive polymer not containing at least one non-terminal thiol group, measured at a pH optimum of the total work of adhesion (TWA) of the thiolated polymer.

Claim 108 (Withdrawn) A polymer as set forth in claim 107, said polymer exhibiting a total work of adhesion (TWA) increased by at least 100% relative to a mucoadhesive polymer not containing at least one non-terminal thiol group, measured at a pH optimum of the total work of adhesion (TWA) of the thiolated polymer.

Claim 109 (Canceled).

Claim 110 (New) A polymer as set forth in claim 1, said polymer being selected from the group consisting of: a thiolated copolymer of acrylic acid and divinyl glycol, a thiolated polymer of chitosan, a thiolated polymer of sodium carboxymethylcellulose, a thiolated polymer of sodium alginate, a thiolated polymer of sodium hydroxypropylcellulose, a thiolated polymer of pectin, and derivatives of said thiolated polymers.